



GLOBAL ACCESS LICENSING FRAMEWORK

Every university-developed technology with potential for further development into a drug, vaccine, or medical diagnostic should be licensed with a concrete and transparent strategy to make affordable versions available in resource-limited countries for essential medical care. Licenses are complex and each will be unique. Universities should therefore implement Global Access Policies that adhere to the following five principles:

1. Access to medicines and health-related technologies for all is the primary purpose of technology transfer of health-related innovations.
2. Technology transfer should protect access to the final end product needed by patients (e.g., formulated pills or vaccines).
3. Generic provision is the best way to ensure access in resource-limited countries for products that also have markets in developed countries. Legal barriers to generic production of these products for use in resource-limited countries should therefore be removed. In the cases of biologic compounds or other drugs where generic provision is forecast to be technically or economically infeasible, “at-cost” or other provisioning requirements should be used as a supplement to generic provisioning terms but should never replace those terms.
4. Proactive licensing provisions are essential to ensure that follow-on patents and data exclusivity cannot be used to block generic production. Other barriers may need to be addressed for the licensing of biologics.
5. University licensing should be systematic in its approach, sufficiently transparent to verify its effectiveness, and based on explicit metrics that measure the success of technology transfer by its impact on access and continued innovation.



GLOBAL ACCESS LICENSING FRAMEWORK EXPLANATORY NOTES

Every drug license must contain access provisions.

Access concerns are not limited to diseases such as HIV/AIDS, tuberculosis, malaria, and other communicable diseases. The World Health Organization reports that chronic diseases such as cardiovascular disease, chronic respiratory diseases, cancer, and diabetes made up 60% of the 58 million annual worldwide deaths, 80% of which occur in low and middle income countries. Over three times as many people die annually from cardiovascular diseases as from HIV/AIDS, tuberculosis, and malaria combined.¹ To ensure access for all essential medicines, it is important that every drug, vaccine, and medical diagnostic license contains access provisions.

Universities Allied for Essential Medicines (UAEM) is sensitive to the opinion that generic production is not essential for medicines indicated for “lifestyle” conditions such as hair loss, acne, or erectile dysfunction. However, because it can be difficult to know at licensing time whether a product will eventually have an essential medical use, even products that are originally licensed for lifestyle indications should have access provisions in their license. These provisions should automatically allow for generic production in the event that any new, non-lifestyle use is demonstrated to be effective via a meta-analysis published in a peer-reviewed journal. Lifestyle uses should be defined narrowly.

The Global Access Licensing Framework should apply to all low and middle income countries.

The choice of which countries to include in a license has grave human consequences. Universities, committed to the public good, should err on the side of over-inclusion. Resource-limited countries should be defined to include low and middle income countries on the World Bank's List of Economies.² These classifications are based on gross national income (GNI) per capita and are revised each year on July 1.

Generic provision is the best way to ensure access.

Generic provision of drugs is the most effective means of driving down prices and increasing access.³ There are several reasons that generic provisions should be required in all licenses for products that also have markets in developed countries:

1. Generic provision enlists competitive market forces to develop the cheapest, most efficient ways to get drugs to patients and providers. Generic companies are in the business of supplying a large volume of drugs as cheaply as possible. In contrast, pharmaceutical companies' drug donation programs do not provide an effective long-term solution—charitable providers have

¹ *Preventing Chronic Disease: A Vital Investment*, World Health Organization (2005), http://www.who.int/chp/chronic_disease_report/en/.

² World Bank Data & Statistics, Country Classification, <http://go.worldbank.org/K2CKM78CC0>.

³ *Report to Congress by the U.S. Global AIDS Coordinator on the Use of Generic Drugs in the President's Emergency Plan for AIDS Relief*, PEPFAR (May 2008), <http://www.pepfar.gov/documents/organization/105842.pdf>.



- fewer incentives to drive down their costs and do not have the expertise or distribution networks that are necessary to get drugs to patients in resource-limited countries.⁴
2. Generic provision eliminates the measurement and enforcement problems inherent in “at-cost” approaches.⁵
 3. Generic licensing approaches foster important innovations specific to the developing-world. For example, such approaches allow generic companies to create pediatric and heat-stable formulations of new drugs.⁶

Generic provisions for resource-limited countries will have a negligible financial impact on the pharmaceutical industry.

The financial impact to pharmaceutical companies of allowing generic competition in resource-limited countries is negligible, especially when revenues from royalties on the generics are taken into account. Drugs with a global market generate only a tiny fraction of their revenue in resource-limited countries. For example, the Pharmaceutical Research and Manufacturers of America (PhRMA) estimates that Africa is only 0.4% of their market, China is only 0.4%, and India is only 0.2%.⁷ Consumers in the United States, European Union, and Japan produced 93.2% of all pharmaceutical revenues for new medicines launched between 2002 and 2007.⁸

To ensure a fully competitive market, production of generics should be allowed in any country, so long as the products are sold only in resource-limited countries, as defined above. This approach is consistent with the framework adopted in the World Trade Organization’s Doha Declaration.⁹ Differential appearance and packaging requirements can be used to ensure that products destined for developing world market are not illegally sold elsewhere.¹⁰

A subset of the pharmaceutical industry is increasingly hospitable to controlled licensing of their drugs for generic use in developing world settings. For example, Gilead recently provided an open voluntary license of its important AIDS medication tenofovir to generic producers in India,¹¹ and both Gilead and Johnson & Johnson announced at the 2008 World AIDS conference that they would be willing to donate intellectual property to a new patent pool being created by UNITAID to allow further generic

⁴ E-mail from Daniel Berman et al., MSF, to Robert Lefebvre, Bristol-Myers Squibb (Feb. 8, 2002), <http://www.essentialdrugs.org/edrug/archive/200202/msg00055.php>.

⁵ Amy Kapczynski et al., *Addressing Global Health Inequities: An Open Licensing Approach for University Innovations*, Berkeley Tech. L.J., 20, 1031 (2005).

⁶ *UNITAID and CHAI Announce Lower Prices for AIDS Drugs and Affordable Formulations for Children*, UNITAID (Apr. 28, 2008), <http://www.unitaid.eu/index.php/en/NEWS/UNITAID-and-CHAI-announce-Lower-Prices-for-AIDS-Drugs-and-Affordable-Formulations-for-Children.html>.

⁷ *Industry Profile 2008*, PhRMA, <http://www.phrma.org/files/2008%20Profile.pdf>.

⁸ *The Pharmaceutical Industry in Figures*, European Federation of Pharmaceutical Industries and Associations (2008), p. 5, <http://www.efpia.eu/Content/Default.asp?PageID=559&DocID=4883>.

⁹ *Ministerial Declaration*, World Trade Organization (Nov. 14, 2001), http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_e.htm.

¹⁰ Kevin Outterson, *Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets*, 5 Yale J. Health Pol’y L. & Ethics 193, 261-265 (2005).

¹¹ *Gilead Announces Licensing Agreements*, Gilead (Sep. 22, 2006), http://www.gilead.com/pr_908393.



production of AIDS medications.¹² Even where pharmaceutical companies are initially resistant to a generic production arrangement, universities can and should insist on such terms as critical to the overall licensing goal of getting innovations to patients, just as they now insist on due diligence terms and measurable development milestones to ensure licensed innovations reach wealthier patients in primary markets.

Additional legal barriers exist to prevent access to the end product needed by patients must be removed.

Some universities have argued that simply not patenting their own discoveries in resource-limited countries constitutes a sufficient access policy. However, if a university does **not** include specific access provisions in its license, there are still several ways licensees could block a generic company from producing the drug for use in resource-limited countries:

Follow-On Patents: Licensees can patent many of the incremental developments inherent in turning the basic licensed compound into a finished marketable drug, creating barriers to access. Several kinds of “follow-on” patents exist:

- *Product patents* cover marginal new chemical additions to the original compound, such as those required to make it dissolve.
- *Process patents* cover the techniques, paths, and intermediates that producers use to synthesize the chemical compound at scale.
- *Use patents* cover the use of the drug for a particular indication.

Data Exclusivity: It currently takes years for a generic company to gain the right to refer to the clinical trial data of drugs that are “bioequivalent” to its own, delaying its ability to provide these drugs in developing countries. In order to sell its drugs to the public, an originator pharmaceutical company must show that the drug is safe and effective by performing clinical trials. A generic company, in contrast, can sell a drug without performing such trials by proving that its drug is bioequivalent to a previously approved drug. In order to do so, it must make reference to the originator pharmaceutical company’s clinical trial data. This “right of reference” is limited by law; in the United States, for example, generic companies must wait five years before referring to clinical trials already registered with the FDA. This delay is particularly problematic for drugs that treat diseases like HIV, where resistance to first- and second-line therapies develops rapidly.

There are a number of strategies to address the issues of follow-on patents and data exclusivity, including non-assert clauses, sublicensing agreements, patent pools, data waivers, and grantback provisions.¹³

¹² James Love, *The Health Impact Fund and product monopolies*, Knowledge Ecology International (Nov. 17, 2008), <http://www.keionline.org/blogs/2008/11/17/health-impact-fund-monopolies/>.

¹³ April E. Effort and Ashley J. Stevens, *The Critical Role of Academic Licensing in Promoting Global Social Responsibility* (2008); Kapczynski et al., *supra*; UNITAID Mission (2005), <http://www.unitaid.eu/index.php/en/UNITAID-Mission.html>.



At-cost or other access provisions are sometimes necessary, but they should rarely replace generic provisions.

At-cost provisions, which require the licensee to sell the licensed technology in resource-limited countries for no profit, may be necessary:

1. When the drug, process, technology, diagnostic, or other component of the licensed product is too complex to be feasible for replication and generic production. For example, many biologics may require at-cost provisions.
2. When the demand for the product in resource-limited countries is too small to induce a generic company to enter into production. Causes of a small demand could include a very small affected patient population as in rare genetic diseases, or an isolated or constrained geographic distribution.

For products that have a market in developed countries, at-cost provisions should never replace generic provisions in licenses. For products that only have a market in resource-limited countries—such as those for “neglected diseases” that are primarily prevalent in resource-limited countries—a geographic market division strategy may not be feasible.¹⁴ Licensees for such drugs are likely to be to non-profit entities, public-private partnerships, or other organizations that are already committed to global access, and a comprehensive strategy for ensuring such access should be established working with each licensee on a case-by-case basis.

Additional barriers to access must be overcome for biologics.

While there is a clear paradigm for the production of small molecule generics, there are a number of important issues related to the production of generic vaccines and other biologics that this framework does not address; there are multiple additional barriers—many of which are non-proprietary—that need to be addressed in order to ensure efficient, cost-effective generic development. Complicating this issue is the ongoing debate in the United States Congress regarding the development of a pathway of FDA approval for generic biologics (known as biosimilars or follow-on biologics). It is currently unclear how this debate will be resolved. Because of the evolving nature of the law, the regulations that are in place at the time that a license is executed could be significantly different from those in place at the time that a licensee has completed end-product development. Therefore, to an even greater extent than for small molecules, it is critical to consider access licensing provisions for biologics on a case-by-case basis.

Still, universities that license biologics should follow the same basic principle: generic provision is the best method for ensuring access, and biologic licenses should do as much to facilitate generic provision as possible. In particular, universities should seek commitments from licensees to transfer materials and know-how to follow-on producers when necessary.¹⁵ Where such agreements are impractical or impossible; when they may be insufficient to ensure follow-on provision; and while there remains no established legal pathway for follow-on biologics, at-cost provisioning commitments should be required.

¹⁴ Jean O. Lanjouw, *Ensuring Access to Low-Cost Drugs in a Patent-Protected World*, Development Outreach, World Bank (2006), <http://www1.worldbank.org/devoutreach/february06/article.asp?id=356>.

¹⁵ Sara E. Crager, Ethan Guillen, and Matt Price, *University contributions to HPV vaccines and implications for access in developing countries: Potential models for improving access to university discovered vaccines*, *American Journal of Law & Medicine* 110-132 (forthcoming, 2009).